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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,414	03/24/2004	Michal Eisenbach-Schwartz	EIS-SCHWARTZ21A	3865

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,414	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-18,21-28,30-37,40-48,50-56,58 and 72* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,10,21-23,25,26,40-42 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,7,8,11-18,24,27,28,30-37,43,47,48,50-56,58 and 72.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1-8,10-18,21-28,30-37,40-48,50-56,58 and 72.

DETAILED ACTION

1. The remarks, amendments, declaration, and terminal disclaimer filed 1 November 2006 have been entered. Claims 9, 19 – 20, 29, 38 – 39, 49, 57, 59 – 71 are canceled; claim 72 is new. Claims 1 – 8, 10 – 18, 21 – 28, 30 – 37, 40 – 48, 50 – 56, 58, and 72 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

3. On pp. 20 – 23, applicant argues that the restriction requirement should be withdrawn as the claims now read on a single invention properly linked by a generic claim. Applicant also argues that the claimed invention meets the unity of invention standard set forth in the PCT Rules and MPEP 1800.

Applicant's arguments have been fully considered but they are not persuasive. The claims still read on multiple inventions and require different searches which are not coextensive with one another. Searching all the diseases and conditions, such as the diverse group recited in claim 14, would be very burdensome to the examiner. Furthermore, the claims as written contain several diseases and conditions which are not reasonably linked by a common mechanism. For example, claim 15 explicitly lists opiate tolerance and dependence as being caused or exacerbated by glutamate toxicity. These are not in fact caused or exacerbated by glutamate toxicity, but are caused by repeated exposure to opiates. Additionally, independent claim 1 encompasses multiple inventions, in that it reads on both attenuation of secondary damage, promotion of nerve regeneration, and protection from glutamate toxicity. Dependent claims read on independent and distinct inventions; see for example claim 2 which requires administration to patients having diseases or conditions that have caused primary damage; see also claim 16 which requires administration to patients having psychoses or mood disorders such as depression. Methods of attenuating secondary damage after primary injury are distinct and independent from treating depression. Thus contrary to applicant's arguments, the claims continue to read on multiple independent and distinct inventions.

With respect to the argument that the invention meets the unity of invention standard, applicant's arguments are not on point. The instant application is not the national stage entry of an international application, but rather is a continuation-in-part of a national stage entry. The unity of invention standard applies only to cases filed under 35 USC § 371, not those filed under

35 USC §§ 111 or 120. Therefore for the reasons above the restriction requirement, which was made final in the previous office action, stands.

4. Claims 5, 7 – 8, 11 – 18, 24, 27 – 28, 30 – 37, 43, 47 – 48, 50 – 56, 58, and 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 20 March 2006. Note that while claims 14, 33, and 52 have each been amended to recite "ischemia", which means a lack of oxygen to cells and is sometimes used synonymously with "stroke", in this case the claims do not read on "stroke", which applicant has elected for prosecution. Rather "ischemia" is referred to in each of claims 14, 33, and 52 as a *peripheral* neuropathy, whereas stroke is a *cerebral* hemorrhage or ischemic event.

5. This application contains claims 5, 7 – 8, 11 – 18, 24, 27 – 28, 30 – 37, 43, 47 – 48, 50 – 56, 58, and 72 drawn to an invention nonelected with traverse in the reply filed on 20 March 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

6. Claims 1 – 4, 6, 10, 21 – 23, 25 – 26, 40 – 42, and 44 – 46 are under examination.

Withdrawn Rejections and Objections

7. The following rejections and objections set forth in the previous office action are withdrawn:

A. The rejection for obviousness-type double-patenting is withdrawn in light of the terminal disclaimer.

B. The rejections under 35 USC § 103 are withdrawn in light of the arguments. The examiner agrees that there is not sufficient motivation in the prior art to substitute poly-Glu,Tyr for Cop-1 in the method of Kipnis et al.

Maintained Rejections and Objections

Claim Objections

8. Claims 4, 23, and 42 stand objected to because of the following informalities: they recite non-elected subject matter. Appropriate correction is required.

This objection is maintained for the reasons of record. Applicant argues that an objection of this type may be held in abeyance until a petition on the restriction requirement is decided. However no such petition has even been filed, so the rejection stands.

Claim Rejections - 35 USC § 112

9. Claims 1 – 4, 6, 10, 21 – 23, 25 – 26, 40 – 42, and 44 – 46 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction of the size of ischemia-induced neural damage and decreasing the amount of neuronal cell loss within the retina by administration of poly-Glu,Tyr, does not reasonably provide enablement for promoting nerve regeneration, or for treatment of the full scope of diseases claimed or for protecting nerves from toxicity in all patients with any disease that is merely exacerbated by glutamate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for the reasons of record in the previous office action and explained further herein. In the previous office action, the examiner had rejected these claims because they encompassed, in part, prevention of neural degeneration. As such language has now been canceled from claim 1, this aspect of the rejection is moot. However, the claims stand rejected as they still encompass subject matter considerably broader than that which is enabled by the disclosure.

The claims encompass methods of promoting nerve regeneration. See for example claim 1 lines 2 – 3. The specification discloses that administration of poly-Glu,Tyr to animals with middle cerebral artery occlusion (MCAO), an experimental model of stroke, has "a positive effect on adult neurogenesis in the brain after ischemia" (p. 50 lines 13 – 14). The declaration submitted under 37 CFR 1.132 and attached exhibit indicate that animals treated with poly Glu,Tyr show significantly increased neurogenesis (see paper attached as exhibit C, pp. 12 – 13). Thus in light of the declaration, which describes the results of similar experiments in more detail, the specification is deemed enabling for increasing neurogenesis following stroke by administering poly-Glu,Tyr. However, what is actually claimed is a method of promoting regeneration of nerves. Regeneration is considerably broader than neurogenesis. The latter means the production, or birth, of new neurons, whereas the former reasonably includes bringing dead neurons back to life. The words are not synonymous, and regeneration of

neurons is generally recognized as being impossible. See for example Jackowski (1995. British Journal of Neurosurgery 9:303-317) who teaches that regeneration is essentially not possible. See Jacowski, p. 305, final paragraph, which discusses the "intrinsic inability of CNS neurosn to mount a regenerative response". Note Jackowski also quotes Ramon y Cajal, who says that "Everything must die, nothing may be regenerated" when discussing neurons (see Jackowski, p. 312). Thus as the prior art indicates that regeneration is essentially impossible, and the specification does not disclose actual regeneration of dead neurons, it would take undue experimentation for the skilled artisan to practice the invention commensurate in scope with the claims.

Furthermore, as set forth in the previous office action, treatment of all diseases is not reasonably encompassed by the claims is not reasonably enabled by the disclosure. The examiner indicated that treatment of two specific diseases, ALS and Huntington's disease, were not reasonably enabled by the disclosure. The examiner cited these two diseases as examples of subject matter not enabled, and the list was representative and not exhaustive. In response, applicant argues that since the specification states that "poly-Glu,Tyr may be a candidate for treatment of ALS and other motor neuron diseases" (p. 52) and because ALS is in part characterized by glutamate toxicity, the specification is in fact enabling for treatment of ALS. The examiner disagrees. ALS is well-known to be a complex disease, whose causes are multiple and remain unknown. See for example Al-Chalabi et al. (2000. Current Opinion in Neurology 13:397-405), p. 397, second column. The mechanism may involve glutamate, but the factors relating to disease onset and progression are complex and interrelated (see Al-Chalabi, Figure 1). The reference teaches that many factors, such as copper toxicity, SOD enzyme structure, as well as protein aggregation and glutamate all influence disease progression. While glutamate is one of many factors involved, as the disease is complex and multi-factorial, and the specification does not show actual treatment of any symptoms of ALS but rather offers speculative statements about the possible applicability of the claimed methods to treatment of this disease, what is actually claimed is not in fact enabled by the disclosure.

Additionally, applicant argues on p. 30 of the remarks "that the treatment with poly-Glu,Tyr is intended to cope with the secondary damage/degeneration that follows the primary injury, regardless of the mechanism causing the primary injury." While that may be applicant's desired scope of patent protection, what is actually claimed is considerably broader. Note for example claim 1 which states in the alternative "A method for inhibiting neuronal secondary

degeneration, or for promoting nerve regeneration... or for protecting nerves from glutamate toxicity" (emphasis added). Claim 2 is in fact more limited, as it requires that the patient who receives the treatment actually be suffering from secondary neuronal degeneration caused by a disease or disorder or injury. Claim 21 also requires that the patient be suffering from certain diseases. But claim 1 encompasses protection from injuries which have not yet occurred, and reasonably encompasses treatment of diseases such as Huntington's for which no enablement has been demonstrated and which have different mechanisms than what is disclosed, and thus would not be expected to be amenable to treatment by administration of poly-Glu,Tyr. Claim 10, which depends from claim 1, allows for the patient to have any disease or disorder "caused or exacerbated by glutamate toxicity". See also claim 26, drawn to patients "suffering from an injury disease, disorder or condition caused or exacerbated by glutamate toxicity". Because almost any disorder would be exacerbated by glutamate toxicity, even non-neural disorders such as diabetes wherein having a seizure would hardly be deemed beneficial, the claims read on treating and attenuating an unreasonably large number of diseases for which enablement has not been shown and would not be expected. For the reasons above, and because the complete breadth of what is claimed is beyond the scope of what is disclosed, the enablement rejection stands.

Claim Rejections - 35 USC § 102

10. Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Vidovic (1985. Journal of Immunology 134:3563 – 3568, cited on IDS filed 24 March 2004), as evidenced by Bussiere et al. (2001. In Functional Neurobiology of Aging, Hof and Mobbs (Eds.). pp. 77 - 84.).

This rejection is maintained for the reasons made of record in the previous office action. Applicant argues that since the word "preventing" has been deleted from claim 1, the claim no longer reads on prophylactic administration to patients who have not yet experienced injury. The examiner disagrees. The claim still encompasses "protecting nerves from glutamate toxicity" and "promoting nerve regeneration" by "administering to an individual in need thereof an amount of poly-GluTyr efftive to... protect nerves from glutamate toxicity." This reasonably encompasses prophylactic administration to all individuals, as all individuals are in need of protection from glutamate toxicity. Note that the claim does not require the patient have any particular disease or condition, and that this is in contrast to claims 2 and 10, for example.

With respect to applicant's discussion as to the mechanism of action of the compound, such discussion is not on point to whether or not the method is anticipated. Vidovic teaches administration of the same compound, at the same dose, to a species of the genus of patients now claimed. Thus the claim is anticipated, irrespective of the mechanism of action of the compound. Applicant did not traverse the examiner's determination that the prior art reference by Vidovich actually teaches administration of the dose and compound claimed in claim 1, but rather presented arguments as to whether or not the same patient population now claimed encompasses that disclosed by Vidovic. Applicant's arguments are not persuasive and thus the rejection stands for the reasons of record.

The examiner notes that only claim 1 is subject to this rejection as no other claims reasonably encompass prophylactic administration to all patients. Amending claim 1 to require that patients have experienced stroke would be sufficient to overcome the rejection. Such an amendment may also be sufficient to overcome the rejection under 35 USC § 112, above, as the specification is enabling for reduction of secondary damage following stroke. Note that other claims may remain rejected should they still encompass treatment of any and all diseases exacerbated by glutamate toxicity or any and all forms of memory loss, psychosis, and depression.

Conclusion

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
January 17, 2007

RCH

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER